

REMARKS

Claims 10-15, 17-22, 25-32, 34-38, 46-59, and 61-62 were pending in this application, following entry of the Amendment After Final and continued examination. Claims 12 and 30 have now been canceled and new claims 63 and 64 have been added. New claims 63 and 64 are supported on page 15, lines 16-18 of the specification and do not add new matter. Furthermore, the amendments to claims 46, 47, 52, and 53, to add the language "encoding a protein involved in the catabolism of a nutritional marker" are supported on page 18, lines 10-13. Applicants request reconsideration of the currently pending claims 10, 11, 13-15, 17-22, 25-29, 31, 32, 34-38, 46-59, and 61-64.

On pages 3-4 of the Office Action of December 31, 2003, the Office indicated that it will maintained the provisional rejection of the pending claims under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-23 and 24-38 of copending Application Serial No. 09/973,013. Applicants understand that this rejection will be withdrawn when the claims of the instant application are in condition for allowance and none of the claims of the copending application have been allowed.

The Office made the remaining rejections of the claims under 35 U.S.C. § 112, second paragraph. Specifically, the Office rejected claims 10-22, 46-51, and 58 as being vague and indefinite because it asserted that an essential "selection step" is not present. See Office Action of December 31, 2003, at 5. As amended, independent claim 10 recites step "(4) selecting the molecule of interest that restores enzyme activity by *in vivo* binding between the molecule of interest and the target ligand, which generates the amplified signal in (3)." Therefore, independent claim 10, as well as

claims 11-22, 46-51, and 58, which depend on claim 10, recite a selecting step and are definite. Applicants respectfully request that the rejection be withdrawn.

The Office also rejected claim 10 as being vague and indefinite because it asserted that the phrase "triggering transcriptional activation" is unclear as not indicating what gene is activated. *See id.* at 5. (Applicants respectfully note that this rejection was made of "claim 1", but assume that this rejection is intended to apply to claim 10.) As amended, step (3) of claim 10 recites "amplifying a signal generated by contacting the molecule of interest and the target ligand in (2) with the signal amplification system of (1), wherein the signal triggers transcriptional activation and expression of a reporter gene", and thus makes it clear that a reporter gene is activated. Applicants respectfully request that the rejection of claim 10 be withdrawn.

The Office rejected claims 14 and 27 under 35 U.S.C. § 112, second paragraph, as being vague and indefinite because of the phrase "chosen from adenylate cyclase or guanylate cyclase and a modulating substance." *See id.* at 5. Claims 14 and 27 have been amended merely to clarify that the modulating substance is one embodiment of the embodiments recited in (B) of claim 10 or 25, which include either a second chimeric polypeptide or a modulating substance. Therefore, claims 14 and 27 are definite, and Applicants respectfully request that the rejection be withdrawn.

The Office rejected claims 15 and 32 as using improper Markush language. *See id.* at 5. As amended claims 15 and 32 recite proper Markush language and Applicants respectfully request that this rejection be withdrawn.

The Office also rejected claim 17 as being vague and indefinite because it asserted that the term "quantified by measuring the synthesis of a signaling molecule or

expression of a reporter gene" is unclear. Merely to further prosecution, Applicants have amended this claim to delete "measuring the synthesis of a signaling molecule" and respectfully request that this rejection be withdrawn.

The Office rejected claims 20 and 36 because it asserted that the phrase "protein with a selectable phenotype" is vague. *See id.* at 6. As amended, claims 20 and 36 recite "a protein that confers a selectable phenotype." Applicants request that this rejection be withdrawn.

The Office rejected claims 25-32, 34-38, 52-57, 59, and 61-62 because it asserted that they lack essential steps. *See id.* at 6. Specifically, the Office was "unclear how one can determine activation or ablation of binding based on the application of a given 'substance' when one abolishes transcriptional activation." *Id.* Claim 25, from which all of the other rejected claims depend, clearly identifies the correlation between the results of the assay and the stated goal of the screen. Specifically, the results of the screen provide determinations of expression of the reporter gene, and therefore transcriptional activation and signal production, in the presence and absence of the substance. As stated in the claim, when there is a difference in the signal amplification in the presence and absence of the substance, this difference "indicates that the substance stimulates or inhibits binding between the target ligand and the molecule of interest." Thus, the goal of the screen is achieved in identifying a substance that stimulates or inhibits binding between the target ligand and the molecule of interest. Accordingly, Applicants respectfully request that the rejection be withdrawn.

The Office also rejected claim 25 because it found the phrase "triggering or abolishing transcriptional activation" to be unclear. See *id.* This phrase has been deleted from the claim. The current term, "wherein the signal triggers transcriptional activation and expression of a reporter gene," identifies the gene as a reporter gene. Additionally, this phrase makes the relationship between transcriptional activation and signal amplification clear. Finally, step (4) of the claim, in which a comparison of transcriptional activation in the presence and absence of the substance to determine whether the substance stimulates or inhibits binding between the target ligand and the molecule of interest, provides a correlation between transcriptional activation and the goals of the claimed method. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The Office rejected claims 46 and 52 as having improper Markush language. See *id.* at 7. The Office was also uncertain about the term "fragment thereof". As amended, claims 46 and 52 recite proper Markush language and clearly indicates the elements of the claim. Applicants respectfully request that this rejection be withdrawn.

Finally, the Office rejected claims 48 and 54, asserting that the phrase "the reporter gene encodes resistance to an antibiotic" does not have sufficient antecedent basis. See *id.* at 7. The current claim term "the reporter gene is a gene conferring resistance to an antibiotic" has antecedent basis in the claims from which they depend, claims 46 and 52, because these claims recite "a gene conferring resistance to an antibiotic". Applicants respectfully request that this rejection be withdrawn.

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any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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